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09/429,331	10/28/1999	LISA A. PAIGE	PAIGE=1D	5796

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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/429,331	PAIGE ET AL.	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *135,139,142,144-146,148-153,155,157 and 158* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *135,139, 142, 144-146, 148-153, 155 and 157-158* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claims 135,139, 142, 144-146, 148-153, 155 and 157-158 are pending and under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Rejection

In view of the amendments to the claims and applicants' arguments the 325 USC 112, second paragraph is withdrawn.

Claim Rejections - 35 USC § 101

Claims 135,139, 142, 144-146, 148-153, 155 and 157-158, as amended and newly added, are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter for reasons of record as reiterated below.

The claimed method of predicting the receptor modulating activity of a test compound does not fall into the above statutory subject matter requirement of process of making or using. It is not clear as to the utility of a method which predicts that a compound would have the claimed function using the process steps. It seems that the process of predicting the function of a compound has not been fully developed such that a compound is positively identified to have the asserted function.

The lengthy specification provides only prophetic statements and not a positive description of the claimed method. The court in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966) held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and ***until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.*** Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696.(Emphasis added).

Thus, at the time of applicants' invention the claimed method of predicting whether a compound has the claimed function does not have a patentable utility. It presents simply a wish to know the identity of any material with that biological property. If applicants were merely wishing to predict were whether a compound would possess an effect or activity, then it appears that the method is still incomplete and has not successfully reached a conclusion. It is little wonder that the specification provides only proposals or prophetic statements as to how the method can be accomplished.

Response to Arguments

Applicants argue that the numerous Examples and significant data provided in the specification describe the identification of numerous peptide conformational probes that exhibit differential binding to estrogen receptor in unliganded form versus the form of the receptor when bound to a number of known ligands (referred to in the specification as reference compounds). The specification further describes, including the provision of experimental binding data, the use of these peptide conformational probes to fingerprint the binding of the numerous ligands having known biological activity. In this manner the biological activity of a newly discovered ligand can be predicted by probing the receptor conformation when bound to the newly discovered ligand and comparing the probe binding pattern to that for the known ligands. The ability to probe the conformation of a nuclear receptor, such as the estrogen receptor, by using the peptide conformational probes provided in the instant specification provides valuable information given that the biological function of nuclear receptors is dictated by receptor conformation.

In reply, applicants' arguments above merely reiterated the claims and failed to specifically point out which Examples, from the alleged numerous Examples, in the specification identify the numerous peptide conformational probes. As stated in the last Office action (see above), the numerous Examples applicants refer to are no more than prophetic examples and general statements. The utility of a compound is not a hunting or guesswork as the claimed predicting for a compound function. Rather, that the compound modulator is positively identified as such and is available in that modulating form.

The importance of nuclear receptor conformation to biological activity is stated in the specification, for example, at page 4, page 8 (bottom) to page 9 (top), and page 18. In addition, Applicants provide further evidence of the substantial utility of the claimed methods for predicting nuclear receptor-modulating activity of test compounds by way of 20 journal articles describing the relationship between nuclear receptor conformation and biological activity. See Exhibits A-T. By way of a particular example, Exhibits A and B describe the use of peptide conformational probes to predict the receptor

modulating activity of newly identified estrogen receptor ligands according to the method of current claim 1 of the instant application.

In reply, Exhibits A-T describe specific compounds identified using the specific phage display library to identify compounds. Even with these already specific compounds Exhibit A for example, discloses at e.g., page 2920, col. 2:

> Recently, we have identified a surface on ERa that is exposed only when the receptor is bound to tamoxifen; we have also demonstrated that the introduction into cells of peptides that bind to this surface inhibits the partial agonist activity of tamoxifen (16). This implies that in the presence of tamoxifen, ERa interacts in an ectopic manner with a factor(s) that enables this compound to manifest partial agonist activity. **Formal proof of this hypothesis awaits the identification of proteins that interact with the tamoxifen-specific surfaces and whose over- or under-expression can alter tamoxifen pharmacology.** One protein that may have this unique property has been reported previously and the significance of this observation is **currently under investigation.** (Emphasis added).

Thus, unless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. A patent is not a

hunting license. It is not a reward for the search, but compensation for its successful conclusion.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 135,139, 142, 144-146, 148-153, 155 and 157-158, as amended and newly added are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed method of predicting a compound that modulates a receptor when bound to it is not described in the specification. The disclosure is full of general and prophetic statements as to the numerous and different embodiments of the invention. It is incomprehensible from the numerous embodiments as to what actually are being made or described specifically as it pertains to the present claim method.

Response to Arguments

Applicants merely reiterated their arguments above and rely on the declaration of McDonnell, which relies on exhibits A-B. Thus, the response above is incorporated herein.

Claim Rejections - 35 USC § 112, second paragraph

Claims 135,139, 142, 144-146, 148-153, 155 and 157-158, as amended and newly added are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. In claim 135, step © "the unliganded reference conformation" lacks antecedent basis of support from the preceding steps. Furthermore, it is not clear as to which reference conformation said phrase is referring to. Also "one or more of the reference conformations" is unclear as to the more than one reference conformations being referred to.

2. Claim 135, step (d) is confusing as to the estrogen receptor reference conformations forming a fingerprint for each of the reference compounds. The entire claim 135 is confusing. It seems that either an essential element/step is missing or the use of different terminologies to mean the same thing provides for confusion and ambiguity.

3. Claim 158 is unclear as to which estrogen receptor is being referred to in claim 135.

Double Patenting

Claims 135,139, 142, 144-146, 148-153, 155 and 157-158, as amended and newly added are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2 and 6 of U.S. Patent No. 6,617,114 ('114 Patent) for reasons set forth in the last Office action.

Applicants state that in contrast to Applicants current claim 135, claims 1, 2, and 6 of the '114 Patent are directed to identifying a ligand which inhibits the binding of an estrogen receptor to a binding partner ligand. Claim 1 of the '114 Patent recites a screening step to identify the ligand having the ability to inhibit the binding of the binding partner ligand to the estrogen receptor. In contrast, Applicants' claim 135 is directed to predicting the receptor modulating activity of a test compound through the use of peptide conformational probes rather than identifying an inhibitor of receptor-ligand binding.

In reply, is this simply a difference in semantics? The instant claim method of predicting the modulating effect of a test compound is an obvious variant or encompasses the '411 method of inhibiting binding to estrogen receptor by a compound using both a screening process. It is considered that the '411 inhibitor is encompassed by the instant peptide conformational probe albeit it does not specifically claim (although' disclose) said conformation interaction. The '411 Patent discloses at e.g., Example 11, Methods and Results heading:

> The sequences obtained in the absence of estradiol are shown in Table 11-1. These sequences possibly represent proteins that interact with the unliganded ER such as HSP90 (90 Kda heat shock protein). Two sequences compete with estradiol (FIG. 23). These sequences may bind to the estradiol binding pocket or they may bind to sites that are masked by a change in receptor conformation following binding of estradiol. The antiestrogen 4-hydroxytamoxifen does not inhibit the binding of any of these phage (FIG. 23).

Thus, the terms "identifying" and "predicting" appear merely a difference in semantics. The claims are not read in vacuum but read in the light of the specification. So read, the specification at page 18, lines 9-17 states:

> This method provides a simple and consistent means for ***identifying*** and characterizing modulators of receptor activity, using 'BioKey' oligomers (especially peptides) to

probe receptor conformation. It can be used as a tool in both primary and secondary screens for compounds that modulate the activity of a receptor.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/TERESA WESSENDORF/

Primary Examiner, Art Unit 1639

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
	09/429,331	PAIGE ET AL.	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	